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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BEISNER, WILLIAM H

ART UNIT

PAPER NUMBER

1744

DATE MAILED: 04/08/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/922,013

Applicant(s)

RUTENBERG ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15, 18-20, 23, 24 and 26-29 is/are pending in the application.
- 4a) Of the above claim(s) 1-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-20, 23, 24 and 26-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 December 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03 Jan. 2003 has been entered.

Election/Restrictions

2. Claims 1-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

Drawings

3. The corrected or substitute drawings were received on 11 Dec. 2002. These drawings are acceptable.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 23, 27 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claims 23 and 27, it is not clear how the language of these claims further limits the structure of the device recited in claim 28. While the language may be more specific it is not clear how this claim language further limits the structure of the system which is encompassed by an analytical or imaging apparatus which already is capable of morphological and DNA ploidy analysis of a cell sample. The instant claim language of these claims appears to be a method step and not a clearly defined structural limitation.

With respect to claim 29, use of the language "most suspect atypical cells" is indefinite. The term "most suspect" in claim 29 is a relative term which renders the claim indefinite. The term "most suspect" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Hicken (US 5,184,626).

The reference of Lee et al. discloses a system (500) for detecting precancerous and cancerous cells in a cell population. The system includes an analytical apparatus including imaging (502) and image processing (536). The imaging and image processing components morphologically select individual atypical (abnormal) cells from the cell population (See classifiers 92, 94, and 96 in Figure 4A). Note the reference discloses that at any stage, objects that are classified as normal or artifact are not classified further (See column 10, lines 54-56). After passing through stage 1, 2 and 3, abnormal (atypical) cells are further classified by a means to conduct DNA ploidy quantization of the selected atypical cells (See ploidy classifier 100).

While the reference of Lee et al. discloses a PAP smear-type of analysis, the reference does not disclose the use of a sample collection brush with the system.

The reference of Hicken discloses that the use of a brush means to collect a cell population for cytological analysis is well known in the art (See brush means, 50).

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In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the PAP smear to be used in the system of the primary reference using the sampling brush of the reference of Hicken for the known and expected result of providing a means recognized in the art for preparing a cell sample specimen. The brush of Hicken providing the advantages that multiple sample sites can be combined into a single sample specimen (See column 1, lines 6-9).

With respect to claim 29, in the absence of further positively recited claim language, the three stage classification of the reference of Lee et al. is considered to meet the "most suspect" limitation of claim 29 since it employs a three-stage process for detecting abnormal cells.

9. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Hicken (US 5,184,626) and Rutenberg et al.(US 5,740,270).

The combination of the references of Lee et al. and Hicken has been discussed above.

Claim 18 differs by reciting that the locations of the atypical cells are retrieved by the analytical apparatus for cell-by-cell analysis.

The reference of Rutenberg et al. discloses a system for classification of cells in a cell sample that employs image processing which is similar to that of the primary reference of Lee et al. The reference of Rutenberg et al. discloses that the locations of the cells which are selected as atypical by the primary and secondary classifiers are stored in the computer system (20) such that tertiary classification can be performed by a person trained to detect truly abnormal cells (See column 8, lines 35-60).

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In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the system of the modified primary reference with a tertiary classification means as taught by Rutenberg et al. for the known and expected result of allowing a person trained to detect abnormal cells can confirm the results of the automated classification system.

10. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Hicken (US 5,184,626), Rutenberg et al.(US 5,740,270) and Bacus (US 5,526,258).

The combination of the references of Lee et al., Hicken and Rutenberg et al. has been discussed above.

The above claim differs by reciting that the computer plots a histogram to show DNA ploidy.

The reference of Bacus discloses that when using a computer to perform DNA ploidy, it is conventional in the art to employ histograms to show DNA ploidy of selected cells (See Figures 3-6 and 12).

In view of this teaching, when performing DNA ploidy analysis, it would have been obvious to one of ordinary skill in the art to program the computer so as to display the results in the form of histograms for the known and expected result of providing a conventional means in the art to display DNA ploidy information which has been determined by a computer. This provides a visual indication of ploidy for the operator of the automated system.

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11. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Hicken (US 5,184,626), Rutenberg et al.(US 5,740,270) and Lee et al.(US 5,787,189).

The combination of the references of Lee et al., Hicken and Rutenberg et al. has been discussed above.

Claim 20 differs by selecting atypical cells using reference cells chosen from the same population.

The reference of Lee et al. ('189) discloses that in an automated cell analysis and imaging system, it is known to employ a reference cell classifier which employs reference cells from the population of cells to be classified and employs the reference cells data when determining atypical cells (See column 4, lines 20-26 and column 5, lines 20-29).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a reference cell classifier in the system of the modified primary reference for the known and expected result of providing a means recognized in the art for compensating for differences in slide preparation (See column 1, lines 12-34).

12. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Hicken (US 5,184,626) and Hemstreet, III et al.(US 5,733,721).

The combination of the references of Lee et al. and Hicken has been discussed above.

The above claim differs by reciting that the system further includes the use of molecular diagnostic techniques on the atypical cells.

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The reference of Hemstreet, III et al. discloses that it is known in the art to employ molecular diagnostic techniques when screening cell samples for cancer. See the entire disclosure. The reference discloses that morphological and ploidy analysis techniques can provide abnormal cells which are not cancerous (See column 2, lines 1-16).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to supplement the classification processes of the modified primary reference using a molecular diagnostic technique disclosed by the reference of Hemstreet, III et al. for the known and expected result of providing an additional level of confirmation of cancerous or precancerous cells since morphological and ploidy techniques are capable of indicating abnormal cells which are not precancerous or cancerous.

13. Claims 24, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 6,137,899) in view of Lonky et al. (US 6,258,044).

The reference of Lee et al. discloses a system (500) for detecting precancerous and cancerous cells in a cell population. The system includes an analytical apparatus including imaging (502) and image processing (536). The imaging and image processing components morphologically select individual atypical (abnormal) cells from the cell population (See classifiers 92, 94, and 96 in Figure 4A). Note the reference discloses that at any stage, objects that are classified as normal or artifact are not classified further (See column 10, lines 54-56). After passing through stage 1, 2 and 3, abnormal (atypical) cells are further classified a means to conduct DNA ploidy quantization of the selected atypical cells (See ploidy classifier 100).

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While the reference of Lee et al. discloses a PAP smear-type of analysis, the reference does not disclose the use of a sample collection brush with the system.

The reference of Lonky et al. discloses that the use of a brush means to collect a cell population for cytological analysis is well known in the art (See brush means, 20).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the PAP smear to be used in the system of the primary reference using the sampling brush of the reference of Lonky et al. for the known and expected result of providing a means recognized in the art for preparing a cell sample specimen. The brush of Lonky et al. provides the advantage that it allows collected samples to include cells in addition to spontaneously exfoliated cells (See column 4, lines 5-25).

With respect to claim 29, in the absence of further positively recited claim language, the three stage classification of the reference of Lee et al. is considered to meet the "most suspect" limitation of claim 29 since it employs a three-stage process for detecting abnormal cells.

14. Claims 18 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044)and Rutenberg et al.(US 5,740,270).

The combination of the references of Lee et al. and Lonky et al. has been discussed above.

Claim 18 differs by reciting that the locations of the atypical cells are retrieved by the analytical apparatus for cell-by-cell analysis.

The reference of Rutenberg et al. discloses a system for classification of cells in a cell sample that employs image processing which is similar to that of the primary reference of Lee et

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al. The reference of Rutenberg et al. discloses that the locations of the cells which are selected as atypical by the primary and secondary classifiers are stored in the computer system (20) such that tertiary classification can be performed by a person trained to detect truly abnormal cells (See column 8, lines 35-60).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the system of the modified primary reference with a tertiary classification means as taught by Rutenberg et al. for the known and expected result of allowing a person trained to detect abnormal cells can confirm the results of the automated classification system.

15. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044), Rutenberg et al.(US 5,740,270) and Bacus (US 5,526,258).

The combination of the references of Lee et al., Lonky et al. and Rutenberg et al. has been discussed above.

The above claim differs by reciting that the computer plots a histogram to show DNA ploidy.

The reference of Bacus discloses that when using a computer to perform DNA ploidy, it is conventional in the art to employ histograms to show DNA ploidy of selected cells (See Figures 3-6 and 12).

In view of this teaching, when performing DNA ploidy analysis, it would have been obvious to one of ordinary skill in the art to program the computer so as to display the results in the form of histograms for the known and expected result of providing a conventional means in

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the art to display DNA ploidy information which has been determined by a computer. This provides a visual indication of ploidy for the operator of the automated system.

16. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044), Rutenberg et al.(US 5,740,270) and Lee et al.(US 5,787,189).

The combination of the references of Lee et al., Lonky et al. and Rutenberg et al. has been discussed above.

Claim 20 differs by selecting atypical cells using reference cells chosen from the same population.

The reference of Lee et al. ('189) discloses that in an automated cell analysis and imaging system, it is known to employ a reference cell classifier which employs reference cells from the population of cells to be classified and employs the reference cells data when determining atypical cells (See column 4, lines 20-26 and column 5, lines 20-29).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a reference cell classifier in the system of the modified primary reference for the known and expected result of providing a means recognized in the art for compensating for differences in slide preparation (See column 1, lines 12-34).

17. Claims 23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(US 6,137,899) in view of Lonky et al.(US 6,258,044) and Hemstreet, III et al.(US 5,733,721).

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The combination of the references of Lee et al. and Lonky et al. has been discussed above.

The above claim differs by reciting that the system further includes the use of molecular diagnostic techniques on the atypical cells.

The reference of Hemstreet, III et al. discloses that it is known in the art to employ molecular diagnostic techniques when screening cell samples for cancer. See the entire disclosure. The reference discloses that morphological and ploidy analysis techniques can provide abnormal cells which are not cancerous (See column 2, lines 1-16).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to supplement the classification processes of the modified primary reference using a molecular diagnostic technique disclosed by the reference of Hemstreet, III et al. for the known and expected result of providing an additional level of confirmation of cancerous or precancerous cells since morphological and ploidy techniques are capable of indicating abnormal cells which are not precancerous or cancerous.

Response to Arguments

18. Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.


Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 703-308-4006. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:40am to 4:10pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 703-308-2920. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9310 for regular communications and 703-872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.


William H. Beisner
Primary Examiner
Art Unit 1744

WHB
April 4, 2003